REMARKS/ARGUMENTS

Claims 15, 17-22, and 29-32, and 34-59 are active. Claims 51-57 are pending but have been withdrawn from consideration. Claim 15 has been simplified by removal of the term "diagnosis" and the last part of this claim indicates that the detection of the presence of PrP^{Sc} is indicative of prions, the particles causing prion disease. Support for this clause is found at least at page 8, lines 3-4 of the specification which indicates that prion "particles are comprised largely if not exclusively of PrP^{Sc} molecules". Similar changes have been made to claims 19 and 20. Claims 22, 32, 37, and 42-49 have been revised for clarity. New claim 58-59 substantially track the language of claim 15 and refers to a method of "general diagnosis", a term suggested by the Examiner. Claim 59 has been directed to a method involving Apolipoprotein B. No new matter is believed to have been added. Favorable consideration of this amendment and allowance of this application are now respectfully requested.

The Applicants thank Examiner Horning for the courteous and helpful interview on October 1, 2008. Amendments that would avoid the indefiniteness, description and enablement rejections were discussed. The Applicants were encouraged to delete the term "diagnosis" or alternatively use the term "general diagnosis" in claim 15 to avoid these rejections. Ways to address the prior art rejections were reviewed. The Applicants were asked to explain why Baumann, et al., which indicates that Apo E "influences the content of β-sheet formation" (abstract) and is "involved in the amyloid deposition and fibril formation" (page 78, 1st col., line 4) did not provide a reasonable expectation of success for further enhancing the transition of $PrP^{C} \rightarrow PrP^{Sc}$. Other alternatives, such as limitation of the claims to methods using ApoB (and not ApoE) were also discussed and the Applicants were encouraged to provide information about the variant structures of ApoB, ApoE, and ApoJ to show that these proteins were not structural and functional analogs.

As requested by the Examiner, the Applicants append to this Amendment scientific articles showing the structural and functional differences among different classes of apolipoproteins, including ApoB and ApoE.

Restriction/Election

The Applicants previously elected with traverse **Group I**, claims 15, 17-22, 29-32 and 34-50, directed to a method of prion detection involving apolipoprotein. The requirement has been made FINAL. The Applicants respectfully request that the claims of the nonelected group(s) which depend from or otherwise include all the limitations of an allowed elected claim, be rejoined upon an indication of allowability for the elected claim, see MPEP 821.04.

Rejection—35 U.S.C. §112, second paragraph

Claims 15, 17-22, 29-32, and 34-50 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the amendments above.

Rejection—35 U.S.C. §112, first paragraph

Claims 15, 17, 18, 21, 22 and 29-32 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate enablement. The Applicants believe that this rejection is now moot in view of the adoption of the suggested preambular language in independent claim 15.

Rejection—35 U.S.C. §112, first paragraph

Claims 48 and 49 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. The Applicants submit that this issue is now moot in view of the clarification of these claims.

Rejection—35 U.S.C. §103(a)

Claims 15, 17-20, 30, 35, 38, 40, 43-45 and 50 were rejected under 35 U.S.C. §103(a) as being unpatentable over Soto, et al., Trends Neurosci. 25:390, Baumann, et al., Biochem. J. 349:77, and Huang, et al., PNAS 98:8838, in further view of Clavey, et al., Annal. D; Endocrinol. 459-463. The Applicants respectfully traverse this rejection because the prior art does not suggest or provide a reasonable expectation of success for the invention.

The Applicants respectfully traverse this rejection because the prior art does not suggest or provide a reasonable expectation of success that apolipoproteins, e.g., the ApoE of Baumann, et al., promote the transition of PrP^{C} to PrP^{Sc} which forms prions.

Soto, et al. describe "Cyclic amplification of protein misfolding" and its application to prion-related disorders (title). However, this document does not suggest that ApoE promotes the transition of PrP^{C} to PrP^{Sc} associated with prion disease or provide any motivation for use of such apolipoproteins in such a cyclic amplification method.

Baumann indicates that ApoE promotes the process of amyloid fibril formation associated with amyloidoses which is a distinct biological phenomenon from the transition of PrP^{C} to PrP^{Sc} associated with prion disease. Furthermore, Baumann is directed to use of ApoE and is silent with respect to the effects of other apolipoproteins on amyloid fibril formation as well as on the transition of PrP^{C} to PrP^{Sc} associated with prion disease (which is not taught at all).

Similarly, Huang, et al. is directed to the role of ApoE fragments in forming "neurofibrillary tangle-like intracellular inclusions" in Alzheimer's Disease (see Title and Abstract) and does not disclose or suggest a role for ApoE in promoting the transition of PrP^{C} to PrP^{Sc} associated with prion disease.

Clavey was applied as teaching that ApoE binds to LDL receptors and specifically with regard to dependent claims 30, 35, 40 and 50. However, like the documents above, it

does not suggest that ApoE or other lipoproteins promote the transition of PrP^{C} to PrP^{Sc} associated with prion disease.

Accordingly, this rejection may now be withdrawn, because the prior art does not disclose, suggest or provide a reasonable expectation of success for the claimed methods which involve use of apolipoproteins to promote the transition of PrP^{C} to PrP^{Sc} associated with prion disease.

Rejection—35 U.S.C. §103(a)

Claims 20, 44, 46, and 47 were rejected under 35 U.S.C. §103(a) as being unpatentable over Soto, et al., Trends Neurosci. 25:390, Baumann, et al., Biochem. J. 349:77, and Naslavsky, et al., JBC 272:6324, in further view of Clavey, et al., Annal. D; Endocrinol. 459-463. Soto, Baumann and Clavey have been discussed above and do not disclose or suggest a method involving use of lipoproteins to promote the transition of PrP^{C} to PrP^{Sc} associated with prion disease.

Naslavsky describes detergent-insoluble complexes containing PrP^{C} as well as PrP^{Sc} with the scrapie form PrP^{Sc} being formed "through the pathological refolding of PrP^{C}," (abstract). However, there is no suggestion is this document either that ApoE promotes a transition from one form to the other.

Therefore, these documents cannot provide a reasonable expectation of success for the present invention

Allowable Subject Matter

The Applicants thank Examiner Horning for indicating that the subject matter of claims 21, 22, 29, 31, 34, 36, 37, 39, 41, 42, 48, and 49 is allowable.

Conclusion

This application presents allowable subject matter and the Examiner is respectfully requested to pass it to issue. The Examiner is kindly invited to contact the undersigned should a further discussion of the issues or claims be helpful.

Respectfully submitted,

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